

Epitomes

Important Advances in Clinical Medicine

General Surgery

The Scientific Board of the California Medical Association presents the following inventory of items of progress in general surgery. Each item, in the judgment of a panel of knowledgeable physicians, has recently become reasonably firmly established, both as to scientific fact and important clinical significance. The items are presented in simple epitome and an authoritative reference, both to the item itself and to the subject as a whole, is generally given for those who may be unfamiliar with a particular item. The purpose is to assist busy practitioners, students, research workers or scholars to stay abreast of these items of progress in general surgery that have recently achieved a substantial degree of authoritative acceptance, whether in their own field of special interest or another.

The items of progress listed below were selected by the Advisory Panel to the Section on General Surgery of the California Medical Association and the summaries were prepared under its direction.

Reprint requests to Division of Scientific and Educational Activities,
California Medical Association, PO Box 7690, San Francisco, CA 94120-7690

New Advances in Pancreatic Transplantation

TRANSPLANTATION OF THE PANCREAS is an effective means of achieving an insulin-independent, euglycemic state in patients with type I diabetes mellitus and, thus, possibly preventing the late renal, vascular and cardiac complications.

Pancreas allotransplantation is being done with increasing frequency and greater success rates. About 1,000 cases have been reported to date, with more than 400 transplants carried out during the period 1983 through 1985, having a one-year success rate of 44%. Over the past two years, with improvements in surgical technique, one-year graft survival rates of 60% to 75% have been reported. With increasing experience, pancreas transplantation has become a safer procedure. At most major centers in the country, the one-year mortality rate for this operation (about 10%) matches that of renal transplants carried out in diabetic patients. While long-term graft survival results are not available, the longest functioning pancreatic allograft reported is eight years.

Various surgical techniques have been used, including transplantation of the entire gland (with or without the duodenum) or of the body and tail (segmental). The "Achilles heel" of the procedure has been management of the exocrine secretions. A diverse number of techniques has been devised, including polymer injection into the pancreatic duct, anastomosis of the duct to recipient bowel or anastomosis of the donor duodenum encompassing the pancreatic duct to recipient urinary bladder. The worldwide experience shows little difference in graft survival rates between these three techniques, while certain centers have yielded excellent results (74% 22-month graft survival) with the urinary drainage technique. This technique has been adopted in most centers in the country today.

Although the technical aspects of pancreas transplantation are difficult, the greatest obstacle to a successful outcome remains immunologic. Registry analysis accompanying var-

ious immunosuppressive therapy protocols shows that graft survival rates are highest (62% at one year for technically successful grafts) with the triple-therapy regimen (low-dose cyclosporine, azathioprine and prednisone). In addition, certain centers are using antilymphocytic globulin prophylactically to decrease the incidence of rejection.

A reliable indicator for the early diagnosis of pancreas graft rejection remains elusive. In patients who have had a simultaneous kidney and pancreas transplant, an elevated serum creatinine level precedes the development of hyperglycemia during a rejection episode of both organs. A distinct advantage of the urinary drainage technique is the ability to follow urinary amylase concentration as a monitor of pancreas graft function. A decrease in urinary amylase often precedes hyperglycemia as an indicator of rejection, and early treatment is initiated on this basis.

PATRICK SOON-SHIONG, MD
GEOFFREY WHITE, MD
Los Angeles

REFERENCES

- Gray DWR, McShane P, Morris PJ: A method for isolation of islets of Langerhans from the human pancreas. *Diabetes* 1984 Nov; 33:1055-1061
- Sollinger HW, Belzer FO, Kalayoglu M: Urinary drainage in pancreas transplantation. *Transplant Immunol Lett* 1986 May; 3:1
- Soon-Shiong P, Swafford G, Levin S: Successful long-term exocrine and endocrine function in the autotransplanted pancreas in man. *Pancreas*, in press
- Sutherland DER, Kendell D, Goetz FC, et al: Pancreas transplantation. *Surg Clin North Am* 1986 Jun; 66:557-582
- Valente U, Arcuri V, Barocci S, et al: Islet and segmental pancreatic autotransplantation after pancreatectomy: Follow-up of 25 patients for up to five years. *Transplant Proc* 1985 Feb; 17:363-365

Alternatives to Total Mastectomy for Carcinoma of the Breast

MORE THAN 90 YEARS AGO Halsted introduced the radical mastectomy as the first rational approach to the surgical management of breast cancer. This procedure remained the most common operation for carcinoma of the breast until it was replaced by the modified radical mastectomy in which the

pectoralis major muscle is not removed, lessening the postoperative deformity. Because survival is not diminished by preserving muscle, the role of even less deforming techniques has been examined in light of our better understanding of the biology of breast cancer.

Removing the entire breast is based on the multifocality of breast cancer and the potential for involvement of the major lactiferous ducts near the nipple. Radiotherapists have long advocated treatment of the whole breast and nipple with external beam radiotherapy or implants, rather than by total breast removal. Early studies showed a high local recurrence rate with irradiation alone. Combining surgical therapy with irradiation, however, appeared as effective as radical mastectomy.

The medical community had been reluctant to accept these observations for a number of reasons, primarily because these trials were not prospective or randomized and they often relied only on clinical staging of the axilla. The highly variable nature of breast cancer and the number of prognostic factors involved made such studies difficult to evaluate. Recent prospective randomized trials have led to a wider acceptance of less-than-total mastectomy.

Veronesi and co-workers reported the first major prospective randomized trial comparing standard surgical treatment with a combination of a surgical procedure and modern radiotherapy. In this trial, patients were randomly selected for a Halsted radical mastectomy or quadrantectomy with axillary lymph node dissection and postoperative radiation therapy. Quadrantectomy removes the entire breast quadrant containing the tumor, including overlying skin and surrounding normal tissue. All entered into this trial had tumors less than 2 cm, not centrally located and no clinical evidence of axillary lymph node disease—the American Joint Committee on Cancer's tumor-node-metastasis stage $T_1N_0M_0$. All patients had accurate axillary staging by examination of the resected lymph nodes. There is no statistically significant difference in local control with either treatment and no difference in overall survival or disease-free survival in this trial comparing radical mastectomy with a far-less-deforming operation and radiotherapy.

The National Surgical Adjuvant Breast Project (NSABP) reported the findings of a trial that extend the observations of Veronesi and associates. In this trial, eligible patients could have a primary tumor as large as 4 cm with or without palpable axillary lymph nodes ($T_{1-2}N_{0-1}M_0$). Patients were randomly assigned to one of three different treatment modalities: the modified radical mastectomy; segmental mastectomy and axillary lymph node dissection, or segmental mastectomy, and axillary node dissection and postoperative irradiation. Unlike the quadrantectomy, the segmental mastectomy removes only the tumor and a small rim of surrounding normal tissue and is even less deforming. Among the 1,843 women randomly selected in this study, few local recurrences were actually seen in the mean follow-up period of 39 months. The lowest local failure rate is among patients treated with segmental mastectomy and radiation therapy. The actuarial predicted five-year local recurrence rate for segmental mastectomy plus irradiation is 7.7%. Segmental mastectomy

without irradiation, however, has a predicted five-year local recurrence of 27.9%. No significant difference in overall survival or disease-free survival is seen among the three different forms of treatment. A longer follow-up will be necessary to answer the questions related to salvage mastectomy for local recurrences and the late effects of treatment.

These trials clearly show that treatment involving less than mastectomy combined with radiation therapy is effective in patients with T_1 and T_2 carcinoma of the breast. Treatment comprising less than total mastectomy without irradiation has a much higher local recurrence rate but may be acceptable for some patients, particularly the elderly, in whom radiation therapy is not desirable. The cosmetic results are far superior to those from mastectomy, and overall survival appears the same. It must be remembered that in both trials, all patients had infiltrating breast cancer, tumor-free margins at operation, tumors not centrally located and had an axillary dissection. Physicians must select their patients with caution, for there are certain groups who should not be considered for a breast-conserving operation. Patients with clinical multifocality, large tumors, centrally located tumors, involvement of the skin, nipple or areolar complex and inflammatory breast cancer or unusual histologies generally should not be treated in this manner.

ARMANDO GIULIANO, MD
Los Angeles

REFERENCES

- Fisher B: The revolution in breast cancer surgery: Science or anecdotalism? *World J Surg* 1985; 9:655-666
- Fisher B, Bauer M, Margolese R, et al: Five-year results of a randomized clinical trial comparing total mastectomy and segmental mastectomy with or without radiation in the treatment of cancer. *N Engl J Med* 1985 Mar 14; 312:665-673
- Veronesi U, Zucali R, Luini A: Local control and survival in early breast cancer: The Milan trial. *Int J Radiat Oncol Biol Phys* 1986 Apr; 12:717-720

Treatment of Renovascular Hypertension

GOLDBLATT 50 years ago produced systemic hypertension in dogs by constricting the renal artery. His published report in 1935 was the first to document a causal relationship between renovascular disease and hypertension. This landmark observation is the basis of our modern understanding of renovascular hypertension. It is now well recognized that significant renal artery stenosis may lead to hypoperfusion of renal parenchyma inducing inappropriate overproduction of renin. By means of the renin angiotensin axis, hypertension is produced.

Because renovascular hypertension is relatively uncommon, it is important to appreciate the clinical features that distinguish it from other forms of hypertension. These include severe diastolic hypertension (greater than 115 mm of mercury), an onset of severe hypertension abruptly and at the extremes of life, evidence of systemic atherosclerosis and the presence of an abdominal bruit. Additionally, this disorder appears to have a racial predilection, being more common in whites. Although these features are typical of patients with renovascular hypertension, the absence of one or more features does not exclude the diagnosis. In our experience, the most reliable clinical predictor of the disorder has been severe diastolic hypertension.